REMARKS

Claim 1 has been amended to delete the optional adjuvant ingredient and to change "containing" to "comprising." Claim 1 has been further amended to clarify the nature of the carrier protein. Support for these amendments can be found at pages 6 and 7 of the specification.

Claims 2-13 have been amended to place them in better form for U.S. patent practice.

Claims 6-8 have been further amended to be consistent with the amendment to claim 1.

Claim 9 has been further amended to be consistent with the amendment to claim 1 and new claim 25.

Claims 12 and 13 have been further amended to correct a typographical error. "Cytosine" should be "cytokine" of which granulocyte-marcrophage colony stimulating factor is a known member.

Claims 14-17 have been canceled in accordance with U.S. patent practice. Applicants note that claims 18-20 had been canceled by the Preliminary Amendment filed on 6 December 2001.

Claim 22 has been amended to correct its grammar.

New claim 25 has been added to claim a method of treating non-transmissible chronic disease as supported in original claim 14.

New claim 26 has been added to claim a method of treating AIDS as supported in original claim 16.

New claim 27 has been added to claim the pharmaceutical composition with the adjuvant.

New claim 28 has been added to claim the provisionally elected ganglioside species.

It is submitted that none of the above amendments are new matter and their entry is requested.

In the Office Action mailed 12 April 2005, the Examiner restricted the 24 claims into 67 Groups, most of which have been further restricted into 14 separate subgroups. Applicants provisionally elect Group 24. Applicants further provisionally elect Group C for consideration. Claims 1-11, 21, 22, 27 and 28 read on these Groups. This election is made with traverse.

The present invention is directed to a general method for increasing the immunogenicity of antigens without chemically modifying the antigens, merely by combining the antigen in question with a specifically defined vaccine carrier. Thus, claim 1 is directed to a pharmaceutical composition for potentiating the immunogenicity of low immunogenic antigens. This pharmaceutical composition comprises one or more low immunogenic antigens and a vaccine carrier. The vaccine carrier consists of very small size proteoliposomes (VSSPs). The VSSPs are derived from the Outer Membrane Protein Complex (OMPC) of *Neisseria meningitidis* wherein gangliosides have been incorporated into the OMPC. The pharmaceutical composition may optionally comprise an adjuvant. The invention also relates to the use of this pharmaceutical composition.

As to the nature of the antigen, the invention is not restricted to a particular kind of antigen other than the fact that the antigen has low immunogenicity. The antigen can be a peptide, or a polypeptide, or a protein, or a nucleic acid sequence coding for a peptide, polypeptide or protein, or a complete cell, or a lysate of a cell, or a combination of any one of these kinds of antigens. For example, the low immunogenic antigen can be a growth factor receptor, such as HER-1, HER-2, PDGF-R and variations thereof.

Thus, it is clear from this brief synopsis of the present invention that all of the alleged antigens, gangliosides, adjuvants and diseases or conditions treated are all directed to the same inventive concept, i.e, the potentiating the immunogenicity of low immunogenic antigens.

Initially, Applicants note that they believe that Groups 19-21 are identical, Groups 22-24 are identical, Groups 25-27 are identical, Groups 28-30 are identical, Groups 31-33 are identical and Groups 24-36 are identical. Applicants therefore believe that the restriction requirement must be reevaluated.

In addition, Applicants note that the Examiner contends that restriction between Groups 1-40 and Groups 41-67 is proper if the product can be used in a materially different process. The Examiner then asserts that the pharmaceutical composition can be used for affinity chromatography. However, Applicants note that the claimed pharmaceutical composition does not contain a single antigen that might be able to be used for affinity chromatography. Instead, the pharmaceutical

composition comprises one or more low immunogenic antigens and a vaccine carrier, which itself is immunogenic. Applicants submit that such a pharmaceutical composition would not be used for affinity chromatography. Thus, the Examiner has not provided a sufficient "materially different process," and the restriction between Groups 1-40 and 41-67 must be reevaluated.

The Examiner also contends that Groups 1-40 are related as combination and subcombination. The Examiner asserts that the patentability of the combination does not rely on the patentability of one subcombination. The basis for this assertion is the fact that the subcombinations are claimed separately. However, Applicants submit that the fact that subcombinations are separately claimed does not *per se* suggest anything about patentability of the combination versus the subcombinations. Claim 1 is directed to a genus, i.e., a composition comprising a low immunogenic antigen and a vaccine carrier, as well as optionally an adjuvant. The genus is expressed as a Markush group in claim 2. The Markush group is a group of related substances, particularly in the immunogenic art. The Markush group is not a subcombination. Thus, the Markush group must be examined together. Similarly, the vaccine carrier is comprised of a Markus group, i.e., gangliosides, and this Markush group is expressed in claim 8. This Markush group is also not a subcombination, and must be examined together.

Furthermore, Applicants note that the field of search for each of the Groups is co-extensive. Specifically, all of the Groups are classified in Class 530, subclass 350 and in Class 424, subclasses 1.11 and 1.21. Thus, a search of these subclasses will encompass all of the alleged Groups.

At best, Applicants submit that the Examiner may be argue that the specified antigens, gangliosides and/or diseases/conditions may be patentably distinct. With respect to patentably distinct inventions, there are two criteria for a proper requirement for restriction between patentably distinct inventions: 1) the inventions must be independent or distinct as claimed; and 2) there must be a serious burden on the Examiner if restriction is not required. See MPEP § 803. Examiner's must provide reasons and/or examples to support their conclusions. For purposes of the initial requirement, a serious burden on the Examiner may be *prima facie* shown if the Examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field

of search as defined in MPEP § 808.02. That *prima facie* showing may be rebutted by appropriate showings or evidence by Applicants. As discussed above, Applicants have shown that the field of search for all of the Groups is co-extensive which means that there is not a separate classification, separate status in the art or a different field of search. Thus, Applicants submit that there is no serious burden on the Examiner to search all of the Groups together.

Insofar as the criteria for restriction practice relating to Markush-type claims is concerned, the criteria are set forth in MPEP § 803.02. See MPEP § 803. According to the MPEP, if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the Examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. In such a case, the Examiner will not require restriction. See MPEP § 803.02. For the reasons discussed above with respect to the various Markush groups encompassed by the claims, Applicants submit that a search and examination can be made of the entire claim without a serious burden, and thus the Groups should be examined together.

Even if the Examiner could support her position that the members of the Markush groups may be distinct from each other, such distinctness alone is not enough to require a restriction as set forth in the MPEP . There must also be a serious burden upon the examiner. In the absence of such a burden, the Examiner must examine all of the claims. It is urged that the burden of examining all of the Groups is not a serious one, and that the burden of examining all of these claims is only slightly greater than examining one of the groups of claims.

The examination entails various aspects. First is a decision concerning utility under 35 U.S.C. §101. Even if each member of the Markush groups could be considered distinct, they are all related in that they are either low immunogenic antigens, gangliosides or diseases/conditions. Consequently, a decision concerning utility will be identical for all of the species, and there is no added burden of examining all of the species as compared to examining only a single species.

The second aspect of examination is whether the provisions of the various paragraphs of 35 U.S.C. § 112 have been met. In general, and in this case, this means reviewing the application and

claims for compliance with the provisions of paragraphs 1 and 2 of § 112. As for the enablement aspect as found in paragraph 1 of § 112, all of the member of the Markush groups are related as noted above. Since no basis for distinguishing between the enablement of one species vs. another species has been set forth, it is presumed that all of the listed members of the Markush groups will be treated equally. Again, this means that only a single decision needs to be made concerning all of the members of the Markush groups . Therefore, this aspect of the examination will not be a serious burden if all members of the Markush groups are examined, vs. only one of the members of the Markush groups .

Concerning paragraph 2 of § 112, this involves the wording of the claims. The wording of the claims in each group of claims is identical except for the specified members of the Markush groups. Consequently, any objections to the language of the claims for one Group of claims is equally applicable to the other Groups of claims. Therefore there is no increase in the burden concerning 35 U.S.C. § 112, second paragraph, if all members of the Markush groups are examined.

The third aspect of examination is a review of prior art to determine whether the claims are anticipated or obvious. There are two aspects of such a search. A first aspect is a review of the prior art literature and patents. The literature to be reviewed will be identical for all of the members of the Markush groups, as evidenced by the Examiner's identification of the field of search. All of members of the Markush groups are related and all are claimed to have the same utility. The Examiner has not stated that a search of the scientific literature will be any different for one member of the Markush groups than for any other member of the Markush groups. Consequently, the search of the patent literature will clearly be the same for all of the members of the Markush groups. Because the search of the scientific literature and patent literature will be identical for all of the members of the Markush groups, there is no added burden concerning this aspect if all of the members of the Markush groups are examined. Consequently, it is submitted that the only reason for restriction is that the members of the Markush groups may be considered to be distinct from each other. But as explicitly stated in MPEP § 803, the inventions must be distinct and there must be a serious burden on the examiner. MPEP § 803.02 states that if a search and examination of an entire

claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. As urged above, it is asserted that examination of all of the members of the Markush groups will not impose a serious burden.

In view of the above arguments, it is requested that the restriction requirement imposed in the Office Action mailed 12 April 2005 be reconsidered and that all of the Groups be examined together.

Respectfully submitted,

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